

Research Article

Qiu Jianmin*, You Xueliang, Liu Liqin, Wu Yongsheng, He Licang, Huang Yuanxin

Value of continuous video EEG and EEG responses to thermesthesia stimulation in prognosis evaluation of comatose patients after cardiopulmonary resuscitation

<https://doi.org/10.1515/med-2018-0006>

received April 5, 2017; accepted November 11, 2017

Abstract: Objective: To investigate the clinical value of video-electroencephalography (VEEG) and thermal stimulus on evaluating the prognosis of comatose patients after cardiopulmonary resuscitation. Methods: Twenty eight comatose patients with cardiopulmonary resuscitation were included in the department of ICU of the First Teaching Hospital of Fujian Medical University from February 2013 to March 2016. Of the included 28 patients, 20 cases died (death group) and 8 cases survived (survival group) after cardiopulmonary resuscitation. The VEEG, Glasgow Coma Scale (GCS) and APACHE II score were recorded and compared between the death and survival group. The prediction value of death for VEEG, GCS and APACHE II were evaluated through sensitivity, specificity and area under the receiver operating characteristic (ROC) curve (AUC). Results: GCS and APACHE II score were statistical different between the death and survival group ($P < 0.05$). With the increase of VEEG grading, the mortality rate of patients increased significantly ($P < 0.05$). Predicting value of mortality for GCS, VEEG and APACHE II were 57.69%, 61.54% and 71.43% respectively without statistical difference ($P > 0.05$). The death prediction sensitivity and specificity for GCS were 67.0% and 85.0%, for APACHE II were 95.1% and 85.0%, for VEEG were 100.0% and 85.2%.

VEEG has the highest sensitivity, Specificity, coincidence rate and Kappa vale compared to GCS, and APACHE II. Conclusion: Video-electroencephalography is a useful tool for predicting the death risk for patients who received cardiopulmonary resuscitation.

Keywords: Video-electroencephalography; Cardiopulmonary resuscitation; Electroencephalography reactivity; prognosis

1 Introduction

The success rate of cardiopulmonary resuscitation (CPR) is significantly improved because of the development of emergency medicine [1]. An increasing number of patients with cardiac arrest are sent to the intensive care unit (ICU) for further treatment after successful cardiopulmonary resuscitation. However, the prognosis of these patients was poor with high death risk [2]. Clinical researches have focused on developing methods for effectively evaluating the prognosis of patients after CPR to apply the limited medical resources to patients worthy of treatment and reduce the burden on society and their families [3]. As an effective indicator of total brain function, electroencephalogram (EEG) is sensitive to cerebral ischemia-hypoxia and metabolic disturbance. This test offers the following advantages: (1) convenient and easy to use for bedside examination; (2) multiple check-ups similar to clinical examination; (3) not relying on the results of clinical examination to evaluate the conscious states of patient [4]. A previous study on the prognostic effects on comatose survivors with cardiac arrest reported that mortality risk can be predicted using EEG responses to external stimulation; the false positive rate (FPR) of the test is 0.07% and could be considered a separate predictive

*Corresponding author: Qiu Jianmin, Department of Neurology, the First Teaching Hospital of Fujian Medical University, Putian 351100, China. No.449 Namenxi Road, Chengxiang District, Putian City, Fujian Province, 351100 PR China. E-mail: qiuying_third@126.com

You Xueliang, Liu Liqin, Wu Yongsheng, Department of Neurology, the First Teaching Hospital of Fujian Medical University, Putian 351100, China

He Licang, Huang Yuanxin, Department of Emergency, the First Teaching Hospital of Fujian Medical University, Putian 351100, China.

factor of case fatality rate (CFR). In recent years, video EEG (VEEG) has been increasingly used to evaluate the prognosis of patients with conscious disturbance; nevertheless, the use of VEEG reactivity for prognosis determination of comatose patients after CPR has been rarely reported.

This study aims to discuss the value of VEEG to thermesthesia stimulation in evaluation the prognosis of patients and provide scientific basis for clinical decision making.

2 Materials and methods

2.1 Patients inclusion

This study retrospectively analyzed 28 comatose patients, who were admitted to our ICU department or related inpatient departments after successful CPR from February 2013 to October 2016. The patients included 16 males and 12 females aged from 21 to 82 years, with a mean age of (48.3 ± 13.1) years. Among this population, 20 patients died (death group) and 8 survived (survival group). The inclusion criteria are as follows: (1) patients aged 18–90 years; (2) patients in a coma state after successful CPR (Glasgow Coma Score ≤ 8 points); (3) patients with family members who provided signed informed consents, which were submitted to the hospital's Ethics Committee for consideration and approval. The exclusion criteria are as follows: (1) patients using sedatives or anesthesia affecting brain electrical activities within 24 h before monitoring; (2) patients with cerebral injury before CPR; (3) patients with high fever, low temperature, and blood circulatory disorder affecting brain electrical activities.

Ethical approval: The research related to human use has been complied with all the relevant national regulations, institutional policies and in accordance the tenets of the Helsinki Declaration, and has been approved by the authors' institutional review board or equivalent committee.

2.2 Methods

This study adopted the Nicolet One-type digital video EEG monitoring system and information processing system. According to the International 10-20 System, scalp electrodes are placed on the patient and electrode paste is used to fix the circular electrode. Based on specific situations, the VEEG recording takes samples from 8 or 16 uni-

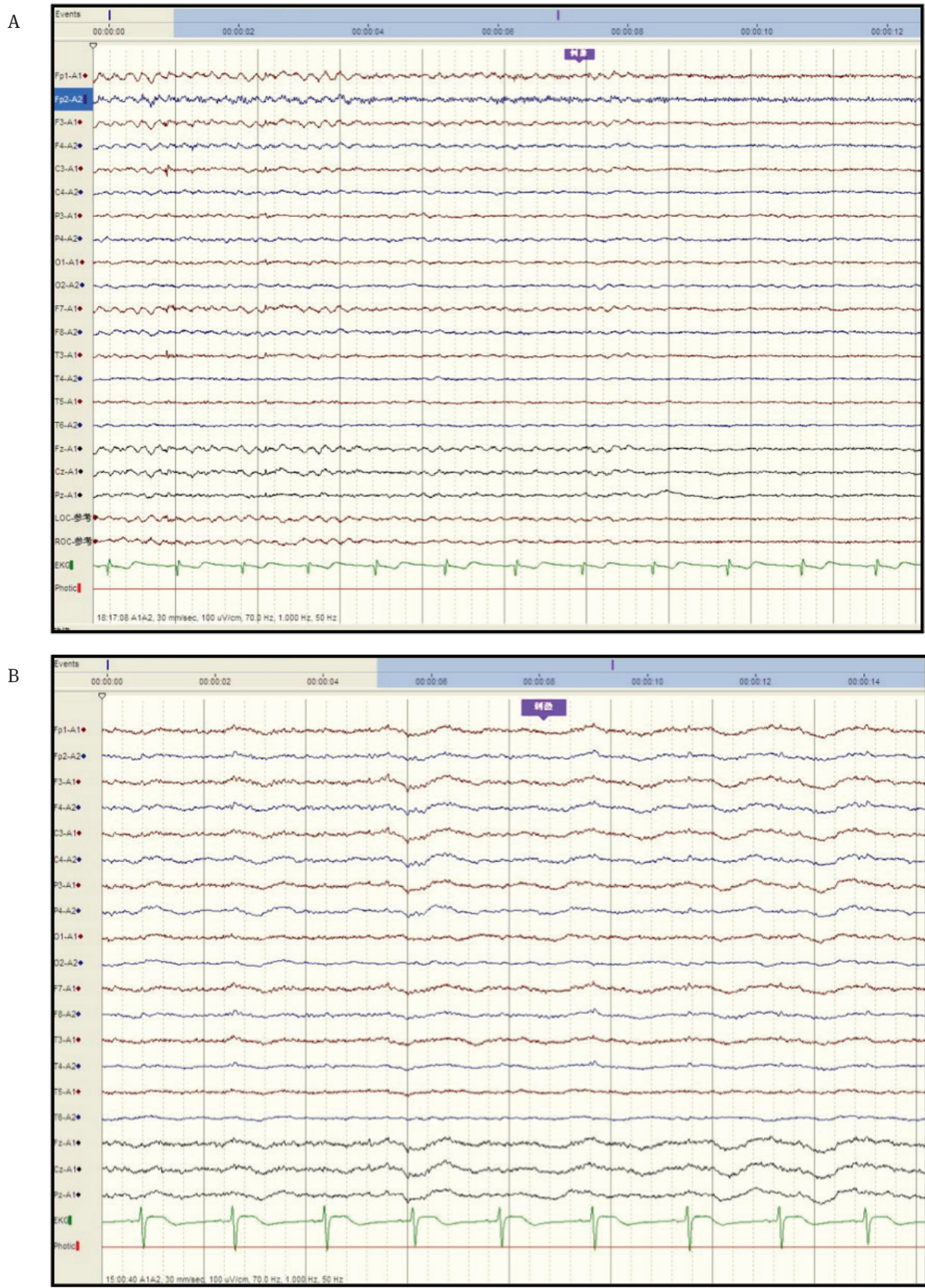
polar leads. The first VEEG recording is completed within 24 h after hospital admission, and each VEEG recording lasts for 6 h every other day, ending with patients' death or the 14th day after morbidity. During VEEG recording, caloric stimulation test is carried out for patients under stable condition. Cold stimulation refers to stimulating patients by ice water with temperature of 0 °C. The two-side upper limb of patients was placed into ice water for 5 s at 5 min intervals, and the process is repeated three times. Real-time changes in VEEG are monitored within 10 s before and after stimulation. Thermal stimulation refers to stimulating patients by using water with temperature of 43 ± 2 °C. Thermal stimulation is performed similar to that of cold stimulation. Two trained physicians, who need to arrive at a consensus after discussion if the judgment is inconsistent, analyze all VEEG recordings. VEEG results are examined using Young grading standard [5]; Grades I and II represent benign VEEG, which predicts patient survival, and the other grades represent malignant EEG, which predicts the death of patients. VEEG reactivity is defined as changes in the frequency or amplitude of VEEG background activity after stimulation; this index exhibits a strict time-locked relationship to the above stimulation but excluding rhythmic, periodic, or irritating discharge and VEEG interference evoked by stimulation. VEEG reactivity is classified into presence and disappearance [6] (Figure 1).

2.3 GCS and APACHE II score

Two independent physicians evaluated GCS and APACHE II score. Glasgow score was a method of assessing the degree of coma with the score less than 5 indicating poor prognosis. APACHE II score is generally used to assess the severity of patients with critically ill patients. APACHE II score is correlated with the death risk. Generally the cut-off value of APACHE II is 16 for poor or good prognosis of critically ill patients [7].

2.4 Statistical method

Data were analyzed with stata11.0 statistical software package. Measurement data are expressed as mean \pm standard deviation. The difference between survival and death patients were assessed by student-t test. Relative number expressed the enumeration data, and the comparison between groups was made based on the chi-square test. Diagnostic sensitivity and specificity was calculated by the equation of $\text{sensitivity} = \frac{\text{true positive}}{\text{true positive} + \text{false negative}}$



tive+false negative), specificity=true negative/ (true negative+false positive). The area under the receiver operating characteristic (ROC) curve was used to evaluate the diagnostic efficacy.

3 Results

3.1 APACHE II and GCS score comparison between survival and death groups

GCS score were 2.76 ± 1.92 and 6.86 ± 1.33 for death and survival group respectively with statistical difference ($P<0.001$); For APACHE II score, the death group was significant higher than those of survival group (23.89 ± 6.75 vs 16.20 ± 4.81 , $P<0.001$), Table 1.

3.2 Correlation between VEEG grading and death risk

With the increase of VEEG grading, the mortality rate of patients increased significantly ($P<0.05$), as shown in Table 2.

3.3 Predicting value of mortality for GCS, VEEG and APACHE II

Predicting value of mortality for GCS, VEEG and APACHE II were 57.69%, 61.54% and 71.43% without statistical difference ($P>0.05$), as shown in Table 3.

3.4 ROC of GCS, VEEG and APACHE II for prediction mortality risk

As shown in Figure 2, the prediction efficacy of mortality in VEEG is better than GCS and APACHE II.

3.5 The prognostic prediction of GCS, VEEG and APACHE II

The sensitivity, specificity, coincidence rate and kappa value for GCS, VEEG and APACHE II were demonstrated in Table 4. VEEG has the highest sensitivity, specificity, coincidence rate and kappa value compared to GCS, and APACHE II.

4 Discussion

After CPR, some patients are subject to serious coma due to cerebral injury caused by respiratory and cardiac arrests. The sign of successful CPR is recovery to cardiopulmonary function; in addition, cerebral survival and recovery of cerebral function are significant for treatment and improving the quality of life of patients. The prognosis of patients can only be judged correctly if the status of cerebral function at the moment is evaluated in a timely and effective manner. Cerebral function is generally evaluated clinically by GCS, APACHE II score system, and biochemical examination combined with neuroimaging; however, these methods are not conducive to bedside monitoring and dynamic observation [8]. VEEG can record the spontaneous bioelectric activities of brain cells from the scalp, reflect the status of electric activities of neuron network in time and space sequences, directly show brain metabolism, and reveal abnormal situations that are difficult to discover [9]. The reactivity of the VEEG background represents good prognosis (especially for survivors after CPR), but guidelines for detecting VEEG reactivity have not been reported. The VEEG reactivity of comatose patients include visualization and auditory stimulation or pain stimulation, which are difficult to quantify in clinical practice; such stimulation may also cause deviations in evaluation, resulting in reduced sensitivity and specificity of VEEG reactivity in prognostic evaluation[10]. Thermesthesia and algesia possess the same nerve conduction pathway (spinal cord–thalamus–cortical pathway), but the former can be easily quantified. In this regard, the present study adopts quantifiable thermesthesia stimulation to improve the accuracy and operability of prognosis evaluation for patients. Video EEG can directly eliminate

Table 1: Comparison between the APACHE II and GCS of survivors and non-survivors

Evaluation methods	Total score	Death group	Survival group	P value
GCS	5.26 ± 2.18	2.76 ± 1.92	6.86 ± 1.33	<0.001
APACHE II	21.56 ± 8.26	23.89 ± 6.75	16.20 ± 4.81	<0.001

Table 2: Relationship between VEEG grading and mortality

Grading	No.	Death (n)	Survival (n)	Death rate (%)
I	3	0	3	0
II	2	0	2	0
III	4	3	1	75
IV	7	6	1	85.71
V	6	5	1	83.33
VI	6	6	0	100
χ^2				33.720
P				0.000

Figure 3: Comparison of the mortality rate between the three evaluating model

Evaluation methods	Acute death (%)	Predict death (%)
GCS	19(67.86)	15(57.69)
VEEG	19(67.86)	16(61.54)
APACHEH II	19(67.86)	20(71.43)
χ^2	2.72	
P	>0.05	

Table 4: Comparison of three methods for evaluating the prognosis of patients with cardiopulmonary resuscitation

Evaluation methods	Sensitivity	Coincidence rate	Specificity	Kappa
GCS	67.0%	66.0%	85.0%	0.65
APACHE II	95.1%	66.0%	85.0%	0.79
VEEG	100.0%	67.0%	85.2%	0.83

EEG identification errors caused by external disturbance and instantaneously observe VEEG reactivity to stimulation. Thus, VEEG provides accurate information for prognosis evaluation of comatose patients and avoiding high medical and economic expenses in patients who will fail to survive or present poor treatment outcomes. The VEEG model after the initial short-term CPR offers limited value in prognosis evaluation. The epileptic form discharges of childhood patients will appear at a minimum of 6 h post-CPR. In the present study, VEEG is recorded after 6 h but within 24 h upon the completion of CPR [11]. The results show that differences in graded VEEG, GOS, and APACHE score can affect the accurate evaluation of patient survival or death risk. The predicted mortality rate calculated by three evaluation methods approximate the actual mortality rate, and the evaluation effects present no significant

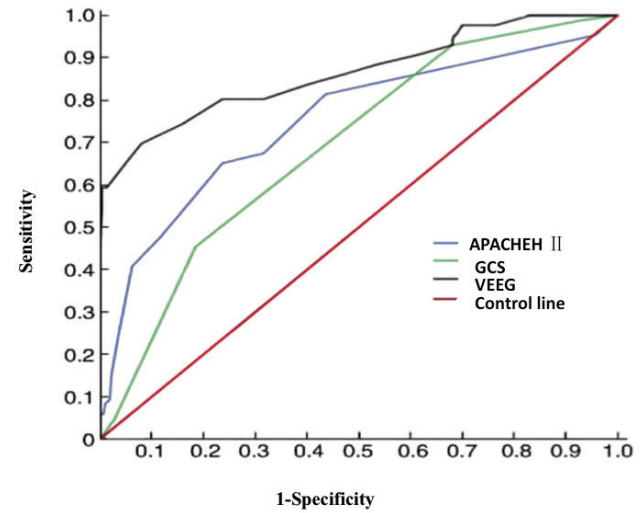


Figure 2: Comparison of ROC curves of three prognostic evaluation methods

differences ($P > 0.05$). Hence, video EEG, GCS system, and APACHE score system present certain clinical value for prognosis evaluation of patients after CPR, consistent with the results of related studies [12]. In addition, the ROC curves of the three prognosis evaluation methods are obtained. The area under the curve (AUC) of video EEG is the largest compared to APACHEII and GCS. However, if a trachea cannula is inserted into a patient’s neck or nose or if the patient is in vegetative state and state of locked-in syndrome, then the scores evaluated by GCS and APACHE may not match with the actual result; nevertheless, these clinical states exert no significant effect on the VEEG-monitored atlas of brain function [13].

VEEG reactivity caused by external stimulation refers to the nervous activity in which somatic sensory afferent pathway passes through the ascending reticular activation system to the cerebral cortex [14, 15]. VEEG reactivity is an important parameter for predicting outcomes of patients with conscious disturbance. After comparing the sensitivity, specificity, and coincidence rate of prognosis evaluation of VEEG reactivity with those of GCS and APACHEII, we observed that the three scores of VEEG for patients after CPR are higher than those of GCS and APACHEII Score. The kappa coefficient is 0.83, which is higher than those of the GOS and APACHE II score system and consistent with follow-up results. During continuous dynamic observation of VEEG, VEEG exhibited no reactivity on the day of morbidity occurrence on two patients, whereas GCS and APACHEII showed poor prognosis. After 2 or 3 days, patients with EEG reactivities ultimately survive. This phenomenon fully demonstrates that VEEG reactivity is an objective and accurate indicator with greater clinical value than other evaluation methods.

Our study possesses several limitations. First, the study was completed in a single hospital and involved a relatively small sample size. The results should be further verified in multiple hospitals with larger sample size. Second, the judgment of VEEG responses to stimulation and VEEG reactivity is subjective to a certain extent and needs to be standardized.

Conflict of interest statement: The authors confirm that this article content has no conflict of interests.

References

- [1] Zhu A, Zhang J. Meta-analysis of outcomes of the 2005 and 2010 cardiopulmonary resuscitation guidelines for adults with in-hospital cardiac arrest[J]. *Am J Emerg Med*, 2016,34(6):1133-1139
- [2] Madl C. [Prognosis for cardiopulmonary resuscitation][J]. *Wien Klin Wochenschr*, 1998,110(20):699-700
- [3] Horn J, Zandbergen EG, Koelman JH, et al. [Prognosis for patients in a coma following cardiopulmonary resuscitation][J]. *Ned Tijdschr Geneesk*, 2008,152(6):308-313
- [4] Schiff ND, Nauvel T, Victor JD. Large-scale brain dynamics in disorders of consciousness[J]. *Curr Opin Neurobiol*, 2014,25:7-14
- [5] Young GB, McLachlan RS, Kreeft JH, et al. An electroencephalographic classification for coma[J]. *Can J Neurol Sci*, 1997,24(4):320-325
- [6] Giacino JT, Hirsch J, Schiff N, et al. Functional neuroimaging applications for assessment and rehabilitation planning in patients with disorders of consciousness[J]. *Arch Phys Med Rehabil*, 2006,87(12 Suppl 2):S67-76
- [7] Su YY, Li HL, Cao GH, et al. The value of APACHE II to predict the outcome of the patients with severe neurologic diseases [J]. *Chinese journal of neurology*, 2008,41(4):258-261
- [8] Søholm H, Kjær TW, Kjaergaard J, et al. Prognostic value of electroencephalography (EEG) after out-of-hospital cardiac arrest in successfully resuscitated patients used in daily clinical practice[J]. *Resuscitation*, 2014,85(11):1580-1585
- [9] Su YY, Wang M, Chen WB, et al. Early prediction of poor outcome in severe hemispheric stroke by EEG patterns and gradings[J]. *Neurol Res*, 2013,35(5):512-516
- [10] Tsuchida TN, Wusthoff C, Shellhaas RA, et al. American clinical neurophysiology society standardized EEG terminology and categorization for the description of continuous EEG monitoring in neonates: report of the American Clinical Neurophysiology Society critical care monitoring committee[J]. *J Clin Neurophysiol*, 2013,30(2):161-173
- [11] Stanko C, Freeman WD. Early EEG correlates of neuronal injury after brain anoxia[J]. *Neurology*, 2012,79(19):2010
- [12] Matic I, Titlic M, Dikanovic M, et al. Effects of APACHE II score on mechanical ventilation; prediction and outcome[J]. *Acta Anaesthesiol Belg*, 2007,58(3):177-183
- [13] Teasdale GM, Murray L. Revisiting the Glasgow Coma Scale and Coma Score[J]. *Intensive Care Med*, 2000,26(2):153-154
- [14] Lin CT, Ko LW, Chang MH, et al. Review of wireless and wearable electroencephalogram systems and brain-computer interfaces--a mini-review[J]. *Gerontology*, 2010,56(1):112-119
- [15] Bazanova OM. [Electroencephalogram alpha activity: modern interpretations][J]. *Usp Fiziol Nauk*, 2009,40(3):32-53